

What is claimed is:

1. A method of making teprenone comprising:
  - (a) reacting geranylgeraniol with an alkyl acetoacetate to form a keto ester intermediate; and,
  - (b) decarboxylating said intermediate to form teprenone.
2. The method of Claim 1, wherein said reacting step comprises:
  - (a) reacting geranylgeraniol with a halogenating reagent to form an alkyl halide; and,
  - (b) reacting said alkyl halide with said alkyl acetoacetate in the presence of a base to form said keto ester intermediate.
3. The method of Claim 2, wherein said halogenating reagent is selected from a member of the group consisting of PF<sub>3</sub>, PCl<sub>3</sub>, PBr<sub>3</sub>, PI<sub>3</sub>, SOF<sub>2</sub>, SOCl<sub>2</sub>, SOBr<sub>2</sub>, and SOI<sub>2</sub>.
4. The method of Claim 2, wherein said halogenating reagent is PBr<sub>3</sub> and the alkyl halide formed is geranylgeranyl bromide.
5. The method of Claim 2, wherein said alkyl acetoacetate is selected from a member of the group consisting of methylacetoacetate, ethylacetoacetate, propylacetoacetate, and butylacetoacetate.
6. The method of Claim 2, wherein said alkyl acetoacetate is ethylacetoacetate.
7. The method of Claim 2, wherein said base is selected from the group consisting of primary amines, secondary amines, tertiary amines, quaternary ammonium salts.
8. The method of Claim 1, wherein said decarboxylating step comprises treating said keto ester intermediate with an alkaline reagent.
9. The method of Claim 2, wherein said alkaline reagent is selected from the group consisting of an aqueous sodium hydroxide solution and an aqueous potassium hydroxide solution.
10. The method of Claim 1, wherein said compound formed contains at least 75% of the 6,10,14,18-tetramethyl-5E,9E,13E,17E-nonadecatetraen-2-one isomer.

11. The method of Claim 1, wherein said compound formed contains at least 90% of the 6,10,14,18-tetramethyl-5E,9E,13E,17E-nonadecatetraen-2-one isomer.

12. The method of Claim 1, wherein said compound formed contains at least 95% of the 6,10,14,18-tetramethyl-5E,9E,13E,17E-nonadecatetraen-2-one isomer.

13. The method of Claim 1, wherein geranylgeraniol is produced biologically.

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14. A method of making teprenone comprising:

- (a) biologically producing geranylgeraniol;
  - (b) reacting said geranylgeraniol with a halogenating reagent to form an alkyl halide;
  - (c) reacting said alkyl halide with said alkyl acetoacetate in the presence of a base
- 5 to form said keto ester intermediate; and,
- (d) decarboxylating said intermediate to form teprenone.

15. The method of Claim 14, wherein geranylgeraniol is produced by a process comprising:

- (a) reacting isopentyl diphosphate with isopentenyl diphosphate:dimethylallyl diphosphate isomerase, in the presence of geranylgeranyl diphosphate synthase to form
- 5 geranylgeranyl diphosphate; and,
- (b) dephosphorylating said geranylgeranyl diphosphate to obtain geranylgeraniol.

16. The method of Claim 14, wherein geranylgeraniol is produced by a process comprising:

- (a) reacting isopentyl diphosphate with a compound selected from the group consisting of dimethylallyl diphosphate, geranyl diphosphate, and farnesyl diphosphate, in
- 5 the presence of geranylgeranyl diphosphate synthase to form geranylgeranyl diphosphate; and,
- (b) dephosphorylating said geranylgeranyl diphosphate to obtain geranylgeraniol.

17. The method of Claim 14, wherein geranylgeraniol is produced by a process comprising:

- (a) culturing a microorganism in a fermentation medium to produce geranylgeraniol;
- and,
- (b) recovering said geranylgeraniol.
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18. The method of Claim 17, wherein said microorganism is genetically modified to decrease the activity of squalene synthase.

19. The method of Claim 17, wherein said microorganism is further genetically modified to increase the activity of HMG-CoA reductase.

20. The method of Claim 19, wherein the activity of HMG-CoA reductase is increased by overexpression of HMG-CoA reductase or the catalytic domain thereof in the microorganism.

21. The method of Claim 20, wherein said microorganism is further genetically modified to increase the activity of a protein selected from the group consisting of acetoacetyl Co-A thiolase, HMG-CoA synthase, mevalonate kinase, phosphomevalonate kinase, phosphomevalonate decarboxylase, isopentenyl pyrophosphate isomerase, farnesyl  
5 pyrophosphate synthase, D-1-deoxyxylulose 5-phosphate synthase, and 1-deoxy-D-xylulose 5-phosphate reductoisomerase.

22. The method of Claim 17, wherein the microorganism has been genetically modified to increase the activity of farnesyl pyrophosphate synthase.

23. The method of Claim 17, wherein the microorganism has been genetically modified to increase the activity of an isoprenoid phosphatase.

24. The method of Claim 17, wherein the microorganism has been genetically modified to increase the activity of geranylgeraniol diphosphate synthase.

25. The method of Claim 17, wherein said microorganism is an *erg9* mutant.

26. The method of Claim 17, wherein said geranylgeraniol is secreted into said fermentation medium by said microorganism and wherein said step of recovering comprises purification of said geranylgeraniol from said fermentation medium.

27. The method of Claim 17, wherein said step of recovering comprises isolating said geranylgeraniol from said microorganism.

28. The method of Claim 17, wherein said step of culturing produces geranylgeranyl pyrophosphate and said step of recovering further comprises dephosphorylating said geranylgeranyl pyrophosphate to produce geranylgeraniol.

